

(FILE 'HOME' ENTERED AT 08:08:40 ON 13 AUG 1998)

INDEX 'AGRICOLA, AIDSLINE, ANABSTR, AQUASCI, BIOBUSINESS, BIOSIS, BIOTECHABS, BIOTECHDS, CABA, CANCERLIT, CAPLUS, CEABA, CEN, CIN, CJACS, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGLAUNCH, DRUGNL, DRUGU, EMBAL, EMBASE, FSTA, GENBANK, ...'

ENTERED AT 08:09:33 ON 13 AUG 1998

SEA LIPSTATIN AND OBESITY

3 FILE BIOTECHABS
3 FILE BIOTECHDS
3 FILE CAPLUS
1 FILE CIN
1 FILE CJACS
2 FILE EMBASE
1 FILE MEDLINE
1 FILE PHIN
2 FILE PROMT
4 FILE SCISEARCH
1 FILE TOXLINE
1 FILE TOXLIT
2 FILE USPATFULL
1 FILE WPIDS
1 FILE WPINDEX

L1 QUE LIPSTATIN AND OBESITY

FILE 'SCISEARCH, BIOTECHDS, CAPLUS, EMBASE, PROMT, USPATFULL, CIN, CJACS, MEDLINE, PHIN, TOXLINE, TOXLIT, WPIDS' ENTERED AT 08:10:16 ON 13 AUG 1998

L2 23 S LIPSTATIN AND OBESITY

L3 16 DUP REM L2 (7 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 08:21:46 ON 13 AUG 1998

INDEX 'AGRICOLA, AIDSLINE, ANABSTR, AQUASCI, BIOBUSINESS, BIOSIS, BIOTECHABS, BIOTECHDS, CABA, CANCERLIT, CAPLUS, CEABA, CEN, CIN, CJACS, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGLAUNCH, DRUGNL, DRUGU, EMBAL, EMBASE, FSTA, GENBANK, ...'

ENTERED AT 08:21:58 ON 13 AUG 1998

SEA LIPASE (15W) INHIBIT? AND ANTIBOD?

1 FILE AGRICOLA
1 FILE ANABSTR
83 FILE BIOSIS
0* FILE BIOTECHABS
3 FILE BIOTECHDS
8 FILE CABA
9 FILE CANCERLIT
76 FILE CAPLUS
11 FILE CJACS
3 FILE DISSABS
3 FILE DRUGU
56 FILE EMBASE
1 FILE FSTA
4 FILE IFIPAT
5 FILE JICST-EPLUS
9 FILE LIFESCI
60 FILE MEDLINE

2 FILE PHIN
2 FILE PROMT
32 FILE SCISEARCH
4 FILE TOXLINE
9 FILE TOXLIT
63 FILE USPATFULL
7 FILE WPIDS
0* FILE WPINDEX
L4 QUE LIPASE(15W) INHIBIT? AND ANTIBOD?

FILE 'BIOSIS, CAPLUS, USPATFULL, MEDLINE, EMBASE, SCISEARCH, CJACS,
CANCERLIT, LIFESCI, TOXLIT, CABA, WPIDS, JICST-EPLUS, IFIPAT,
TOXLINE, BIOTECHDS, DISSABS, DRUGU, PHIN, PROMT, AGRICOLA, ANABSTR,
FSTA' ENTERED AT 08:30:38 ON 13 AUG 1998
L5 856 S LIPASE(15W)ANTIBOD?
L6 4 S L5 AND OBESITY
L7 4 DUP REM L6 (0 DUPLICATES REMOVED)
L8 190 S L5 AND (TREAT? OR THERAPY)
L9 89 DUP REM L8 (101 DUPLICATES REMOVED)

Mode of action of orlistat.

AU Guerciolini R.
CS R. Guerciolini, Div. International Clinical Research, Hoffmann-La Roche Inc., Nutley, NJ, United States
SO International Journal of Obesity, (1997) 21/SUPPL. 3 (S12-S23).
Refs: 42
ISSN: 0307-0565 CODEN: IJOBDP
CY United Kingdom
DT Journal
FS 030 Pharmacology
039 Pharmacy
037 Drug Literature Index
LA English
SL English
AB Gastric and pancreatic lipases are enzymes that play a pivotal role in the digestion of dietary fat. Orlistat, a semisynthetic derivative of **lipstatin**, is a potent and selective inhibitor of these enzymes, with little or no activity against amylase, trypsin, chymotrypsin and phospholipases. It exerts its effect within the gastrointestinal (GI) tract. Orlistat acts by binding covalently to the serine residue of the active site of gastric and pancreatic lipases. When administered with fat-containing foods, orlistat partially inhibits hydrolysis of triglycerides, thus reducing the subsequent absorption of monoacylglycerides and free fatty acids. This effect can be measured using 24 h faecal fat excretion as a representative pharmacodynamic parameter. Orlistat's pharmacological activity is dose-dependent and can be described by a simple E(max) model which exhibits an initial steep portion of the dose-response curve with a subsequent plateau (.apprx. 35% inhibition of dietary fat absorption) for doses above 400 mg/d. At therapeutic doses (120 mg tid with main meals) administered in conjunction with a well balanced, mildly hypocaloric diet, the inhibition of fat absorption (.apprx. 30% of ingested fat) contributes to an additional caloric deficit of approximately 200 calories. Orlistat does not produce significant disturbances to GI physiological processes (gastric emptying and acidity, gallbladder motility, bile composition and lithogenicity) or to the systemic balance of minerals and electrolytes. Similarly, orlistat does not affect the absorption and pharmacokinetics of drugs with a narrow therapeutic index (phenytoin, warfarin, digoxin) or compounds frequently used by obese patients (oral contraceptives, glyburide, pravastatin, slow-release nifedipine).

L3 ANSWER 15 OF 16 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 86-10072 BIOTECHDS
TI Leucine derivatives;
 lipstatin or tetrahydrolipstatin preparation using
 Streptomyces toxytricini; hypolipemic and anorectic
 lipase-inhibitor
PA Roche
PI US 4598089 1 Jul 1986
AI US 84-621827 18 Jun 1984
PRAI CH 83-3415 22 Jun 1983
DT Patent
LA English
OS WPI: 85-007713 [02]
AB Novel leucine derivatives include **lipstatin** (Ia) and
tetrahydrolipstatin. They show pancreas lipase-inhibitor activity
and can be used for the control or prevention of **obesity**
and hyperlipemia. **Lipstatin** is obtained by cultivation
of Streptomyces toxytricini 85-13 (NRRL 15443). Cultivation is
performed in a medium containing C- and N-source plus inorganic
salts at 20-37 deg for 1-6 days. **Lipstatin** is recovered
by conventional methods. For example, the cell mass is extracted
with methanol and ethanol, while the culture supernatant is
extracted with methylene chloride or ethyl acetate. The material
produced from the extracts is subjected to multiplicative
extraction with the system hexane-methanol-water (50:40:9),
filtration chromatography over silica gel eluting with hexane or
ethyl acetate, and chromatography on apolar carriers, eluting with
polar solvents. Tetrahydrolipstatin is obtained from
lipstatin by hydrogenation. (8pp)